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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/325,602 06/03/99 GALDES

A CIBT-P02-069

DOCKETING SPECIALSIT, 33/48
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HM12/0904

EXAMINER

MOEZIE, F

ART UNIT

PAPER NUMBER

1653

DATE MAILED:

09/04/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/325,602

Applicant(s)
Galdes et al

Examiner
F. MOEZIE

Art Unit
1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Jun 14, 2001.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above, claim(s) 5-10 and 12-21 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-4 and 11 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1-21 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

20) ☐ Other:

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DETAILED ACTION

STATUS OF CLAIMS

Claims 1-4 and 11 are pending prosecution in this Office action.

The earlier Restriction Requirement is now made **Final**.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 11 is again objected to as it depends from non-elected claims. Cancellation of non-elected subject matter from the claim is suggested.

REJECTION - 35 U.S.C. 112, FIRST AND SECOND PARAGRAPHS

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 11 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without **undue experimentation**. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to

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consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Foreman*, 230 USPQ 546 (Bd App 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction and guidance provided,
- 3) The presence or absence of working examples,
- 4) The nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art ‘
- 7) the predictability of the art, and
- 8) the breadth of the claims.

Applicant fails to set forth the criteria for selecting a useful “lipophilic *modified hedgehog* polypeptide” among the myriad of modified polypeptides known in the art as evidenced by the specification. Additionally, applicant fails to provide information allowing the skilled artisan to know the necessary degree of lipophilicity for the *modified hedgehog* polypeptides which were be used in the claims. Further, applicant fails to cite the unique properties for the “lipophilic *modified hedgehog* polypeptide” such as; the molecular weight(s) for the polypeptides, the nature, the position (s), the number (s) and the extent of the modification, and the amino acid sequence ID NOS. The instant claims read on all modifications and the determination of a useful “lipophilic *modified hedgehog* polypeptide” for use in the claimed methods necessitate an exhaustive search for determining the useful *modified hedgehog*

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polypeptides and the relative proportions to use in the practice of the claimed invention. Finally, there is no guidance as to how an art skilled would recognize the *modified hedgehog* polypeptide. Hence, it would clearly be an **undue burden** to practice the claimed invention.

The rejection of the claims 1-4 and 11 under **35 U.S.C. 112, second paragraph**, is maintained for the reasons of record, Office action mailed 2/13/01, paper no. 11.

The claims are indefinite regarding their metes and bounds, i.e., which modified hedgehog peptides were used in the methods and how were they modified? The modified polypeptides having; a) an unspecified amino acid sequence(s), b) N- or C- modified hedgehog polypeptides (or is the polypeptide also modified, if so, how?) c) and an unspecified number of lipophilic groups in the polypeptides, and etc. None of the modified hedgehog polypeptides have been identified in the claims or examples (also, none was elected as the specie of choice). Hence, the claims are indefinite as they fail to particularly point out the claims' metes and bounds.

REJECTION - 35 U.S.C. 103 (a)

The rejection of claims 1-4 and 11 under **35 U.S.C. 103 (a)** as being unpatentable over Ingham '079 and/or '543 in view of Pepinsky is maintained for the reasons of record.

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Claims 1-4 and 11 are rejected under **35 U.S.C. 103(a)** as being unpatentable over WO 96/17924 to Beachy et al (specification page 31) and/or US 5,789,543, filed 12/30/93, to Ingham et al in view of Muranishi et al, Journal of Controlled Release, 19:179-188 (1992).

Beachy claims "A method for modulating proliferation or differentiation of neuronal cells, comprising contacting the cells with a hedgehog polypeptide" (claim 17). Moreover, beachy teaches that "N" and "C" fragments of hedgehog polypeptides are known in the art and used for treating disorders of the nervous system. See the entire document, especially page 15, lines 8-20 and the claims.

Ingham teaches that various Shh polypeptides, fragments and the use thereof "to regulate neurogenesis" (col. 3, lines 37-38) is known in the art. Further, '543 teaches that "methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo" are known in the art (Abstract). See, the entire document.

However, the primary references do not teach the use of acylated polypeptide.

The secondary reference teaches that lipid modification of peptides improves the peptides capabilities against enzymatic degradation (abstract). See the entire document.

An ordinary art skilled at the time the invention was made would have been motivated to make a lipophilically modified derivative of the hedgehog polypeptide or fragments thereof according to the teaching of the art for use in the methods of using the polypeptides which are

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also taught by the art for at the very least imparting greater stability against degradation to the resulting compounds - absent evidence to the contrary.

RESPONSE

Applicant's arguments filed 6/14/01, paper no. 13, have been fully considered but they are not persuasive for the following reasons:

Regarding the arrangement of the specification, applicant is reminded that this application is a later application since it is CIP of an earlier application. Compliance is recommended.

The claims remain rejected under 35 U.S.C. 112, second paragraph, for the reasons cited earlier and above. Remarks regarding the *in vivo* applications of lipophilic modified hedgehog polypeptides have been considered. Clearly, scope of a claim is not the subject to be dealt with under the second paragraph, but the metes and bounds of the claim falls under this paragraph and as such, the claims' are indefinite regarding their metes and bounds as further cited above.

The rejection of the claims under 35 U.S.C. 103 as being unpatentable over Ingham et al in view of Pepinsky et al is maintained for the following reasons:

Applicant admits that Ingham addresses the use of hedgehog polypeptides for regulating differentiation of many cell types including neuronal cells (page 4, first paragraph).

Applicants' assessment of Pepinski is not well taken. Note; the document is entitled "Identification of a Palmitic acid-mediated form of Human Sonic Hedgehog". See, also the Abstract, wherein Pepinski declares "The observation that an extracellular protein such as Shh is

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palmitoylated is highly unusual and further adds to the complex nature of this protein” (last sentence). Finally, regarding human Shh the article teaches: “they reveal that NH2-terminal modification above is as effective as the cholesterol modification at enhancing the activity of Shh” page 14044, paragraph bridging the two columns. Remarks regarding the assay test are not well taken since a) the claims are silent in this regard and b) applicant admits that “Such assay is not necessarily an indicator of neuronal development or neuronal survival” page 4, third paragraph. Applicant is reminded that the rejection is based on obviousness and an ordinary art skilled would clearly expect that the modified Shh as taught by Pepenski would have a greater activity in the method as claimed. Finally, arguments regarding “the blood-brain barrier, a requirement for an effective therapeutic agent ---” (page 5 of Remarks) are not applicable herein since, the claims are drawn to treating cells and not treating patients.

Any inquiry concerning this communication should be directed to F.T. Moezie at telephone number (703) 308-4508 or Dr. LOW (SPE) at 308-2923.

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HARRY EXAMINER
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